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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/547,220	04/11/2000	Michael Brines	10165-006-999	4714

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EXAMINER
DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
1647	14

DATE MAILED: 06/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/547,220	BRINES ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,6,11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of Application, Amendments and/or Claims

Attorney Laura A. Coruzzi has stated in the Communication received by the Office 21 May 2002, "based on our conversation, it is our understanding that the U.S. Patent and Trademark Office will rescind the outstanding Office Action dated May 8, 2002, consider the references cited in the Information Disclosure Statement, and issue a new Office Action shortly". Accordingly, the Office Action of 08 May 2002 (Paper No. 13) is hereby vacated and Applicant is relieved of the requirement to respond to that Office Action. The following is a complete action on the merits.

The information disclosure statement, filed 20 November 2000 (Paper No. 4), 10 October 2001 (Paper No. 6) and 05 March 2002 (Paper No. 11) were received and comply with the provisions of 37 CFR §§1.97 and 1.98. They have been placed in the application file and the information referred to therein has been considered as to the merits.

The amendment filed 05 March 2002 (Paper No. 12) has been entered in full. Claims 1-27 were cancelled. Claims 28-34 are under examination. Applicant's election of species recombinant human erythropoietin in Paper No. 12 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The disclosure is objected to because of the following informalities: In the Brief Description of the Figures "FIG. 3A-B" should read "FIG. 3A-C" (page 7, line 9). Appropriate correction is required.

Claim Objections

Claim 33 is objected to because of the following informalities: Claim 33 encompasses a non-elected invention and requires amendment to limit to elected invention. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make

and/or use the invention. Claim 32 is drawn to the method wherein said erythropoietin is administered at a dosage of 50,000 to 100,000 Units per administration or per day.

The instant claim lacks enablement because prior art teaches away from the instant dosages. Sakanaka *et al.* (IDS#4, CH) report that EPO, *in vivo* protects neurons against ischemia-induced cell death. One unit of recombinant human EPO approximately corresponds to 10ng of EPO protein. EPO at a dose of 0.5, 2.5, 5, or 25 units/day was infused for 7 days into the left lateral ventricle of each gerbil (page 4635, material and methods). Sakanaka teaches that EPO at a dose of 50 units/day or 500 units/day was ineffective in preventing the ischemia-induced reduction or response latency and neuronal loss (page 4637, 2nd paragraph and page 4638, 2nd paragraph). Sakanaka suggests that the hippocampal neurons with EPOR respond to EPO within a limited concentration range *in vivo* and that high concentrations of EPO induce a rapid down-regulation of EPOR, failing to transmit EPO-mediated signals to the neurons (page 4638, 2nd paragraph-4639).

A similar experiment using rats was disclosed in example 4 of the instant specification (page 32, line 16-page 33, line 14). The concentration of EPO (units/body weight) used for this particular experiment, however, was not disclosed.

Nissenson *et al.* (IDS#4, BZ) discusses the safety and efficacy of administering rhEPO. Nissenson teaches that rhEPO could correct the anemia of renal failure. However, complications of using rhEPO were seen. Some patients developed severe hypertension with encephalopathy and had seizures. The severe complications

occurred in patients receiving high doses of rhEPO in (>500 U/kg three times a week) and were felt to be related to the rapid rise in the hemacrit (page 407, 2nd paragraph).

Odgen (IDS#4, CA) also discusses the importance of monitoring and establishing therapeutic doses of rhEPO. Odgen teaches that during clinical trial, the most significant side effect of rhEPO therapy discovered to date has been the exacerbation of or de novo hypertension, which has led in a few instances to the severe consequences of seizures (page 13, 1st paragraph)

Therefore in view of the contradictory state of the prior art teaching away from the instant concentrations of erythropoietin employed in methods for administering erythropoietin and the importance of establishing safe therapeutic doses of rhEPO, claim 32 as cited is not enabled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 28 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 is indefinite because the claim must achieve the goal stated in the preamble. The claim does not have a step that clearly relates back to the preamble.

Claim 32 is indefinite because it cites a dosage unit without a body weight for administration.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 28-31 and 33,34 are rejected under 35 U.S.C. 102(b) as being anticipated by Grimm et al. (IDS#4, BC). The claims are mainly drawn to a method for treating cerebral ischemia in a mammal comprising administering erythropoietin peripherally to said mammal. "Treating cerebral ischemia" and "for the treatment of stroke" are the intended uses recited in the instant claims and are not given significant patentable weight. Furthermore, the claims do not require that the mammal suffer from any condition. "Treating" can reasonably be broadly interpreted as encompassing prophylactic treatment in a healthy patient. Grimm's teachings of improvement of brain function by administering erythropoietin do not teach against the intended use cited in the claims.

Grimm teaches administering rhuEPO (recombinant human erythropoietin) to a human. The rhEPO was administered intravenously (peripherally) and vascularly (page 480, 4th paragraph Methods).

The Harper Collins Illustrated Medical Dictionary defines peripheral as pertaining to the outer surface body or situated away from the center. Vascular is defined as pertaining to or containing vessels (please see printout from Harpers Collins). Thus Grimm anticipates the instant claims.

Conclusion

No claims are allowed.

Matter of Record

The art made of record and not relied upon is considered pertinent to applicant's disclosure. Ehrenreich *et al.* WO 00/35475 (IDS#, AR) discloses a method for the treatment of cerebral ischemia (and stroke) in mammals (humans) comprising administering EPO intravenously (peripherally, vascularly). Recombinant human EPO concentrations include 5,000 IU to 100,000 IU per administration and/or per day. Ehrenreich discloses the instant claims. However, the WO 00/35475 reference has an international publication date of 22 June 2000 and thus cannot be considered prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on Mondays-Fridays 8:00 a.m. - 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
June 4, 2002

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER